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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/940,422	08/29/2001	Lorraine Mary Edmeades	1430-272	5500

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EXAMINER

SODERQUIST, ARLEN

ART UNIT	PAPER NUMBER
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1743

DATE MAILED: 07/02/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n N .

09/940,422

Applicant(s)

EDMEADES ET AL.

Examiner

Arlen Soderquist

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☒ Certified copies of the priority documents have been received in Application No. 09/265,670.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: .

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1. The disclosure is objected to because of the following informalities: the parent application and its status should be added.

Appropriate correction is required.

2. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

3. Claims 5-10 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 4-9 of prior U.S. Patent No. 6,333,198. This is a double patenting rejection.

4. Claim 11 provides for the use of a compound as a reference marker in testing the stability of a sample of lamotrigine, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

5. Claim 11 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

6. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the last line of the claim "in the or" is not clear.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

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has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

8. Claims 1 and 11 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Floyd (US 5,942,510). In the patent Floyd teaches a pharmaceutical composition containing lamotrigine. Tables 2 and 3 give results from assays of the compositions for stability. In Table 2, the first column under the related substances is for the compound 3-amino-5-keto-6-(2,3-dichlorophenyl)-1,2,4-triazine (footnote g), which is the instantly claimed 3-amino-6-(2,3-dichlorophenyl)-1,2,4-triazine-5(4H)-one. In Table 3, footnote a teaches that the assay was by High Performance Liquid Chromatography (HPLC) according to the Analytical Standard.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Floyd as applied to claim 1 above, and further in view of Papadoyannis. Floyd does not teach the use of standard solutions.

In the paper Papadoyannis presents an efficient off-line solid-phase extraction (SPE) of lamotrigine (LTG) from human serum and urine prior to HPLC analysis. High extraction recoveries were achieved from C8 bond Elut cartridges (200mg/3ml), using acidic acetonitrile for the elution of LTG and the internal standard, 3,5-diamino-6-(2-methoxyphenyl)-1,2,4-triazine. Isocratic reversed-phase HPLC (RP-HPLC) analysis on octyl silica, using a Lichrosorb RP-8, 5 μ m, 250 \times 4.6 mm column and a mobile phase consisting of pH 5.6 0.05M acetate

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buffer-MeCN (72:28) was sensitive and rapid. The identification of LTG was performed by UV detection at 306nm. The method detected approx. 0.9 ng LTG on-column, using a 20- μ L loop, and linearity holds from ~ 0.044 to $7.8 \mu\text{g/mL}$ in standard solutions. These standard solutions were used to form a calibration chart for determining concentrations and also for checking the day-to-day precision and accuracy. In plasma and urine, the limits of detection are 1.1 and 1.2 ng, respectively, while linearity holds from ~ 0.087 to $3.49 \mu\text{g/mL}$. The proposed method was also used for the direct analysis of antiepileptic tablets.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use standard solutions in the Floyd method because as shown by Papadoyannis the standard solutions allow formation of calibration charts for determining concentrations and checking the day-to-day precision and accuracy.

11. Claims 1-5 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dreassi in view of Floyd and Quaglia or DeAngelis. In the paper Dreassi teaches quantitative analysis of lamotrigine in plasma and tablets by planar chromatography and comparison with liquid chromatography and UV spectrophotometry. A method using planar chromatography (PC) was developed for determining lamotrigine (LTG) in human plasma and in tablets. LTG was extracted with MeCN in the presence of Na_2CO_3 . 3,5-Diamino-6-(2-methoxyphenyl)-1,2,4-triazine was used as internal standard. The detection limit was $0.27 \mu\text{g/mL}$ plasma and the recovery from human plasma fortified with various concentrations of LTG was 91.3%. No interference from other common antiepileptic agents was found. The results obtained with the PC method were compared with those obtained by a method using liquid chromatography for analysis of plasma and tablets. On page 1278 Dreassi teaches the formation of calibration standards and the operating conditions including the method of quantification. Dreassi does not teach the quantification of any impurities.

In the patent Floyd teaches a pharmaceutical composition containing lamotrigine. Tables 2 and 3 give results from assays of the compositions for stability. In Table 2, the first column under the related substances is for the compound 3-amino-5-keto-6-(2,3-dichlorophenyl)-1,2,4-triazine (footnote g), which is the instantly claimed 3-amino-6-(2,3-dichlorophenyl)-1,2,4-triazine-5(4H)-one. In Table 3, footnote a teaches that the assay was by High Performance

Liquid Chromatography (HPLC) according to the Analytical Standard. It is also noted that the preparations also contain other components that are measured, but not identified.

In the paper Quaglia teaches the determination of chlorthalidone and its impurities in bulk and in dosage forms by high-performance thin-layer chromatographic densitometry. Chlorthalidone and its impurities were determined in bulk and pharmaceuticals by high-performance TLC-densitometry with dioxane-iso-PrOH-25% NH₄OH-toluene-xylene (30:30:20:10:10) as the mobile phase. The relative standard deviation was 1.9% and the recovery of chlorthalidone and the impurities from artificial mixtures was 96.4-102.0%. Pages 436-437 teach the preparation of standards for Chlorthalidone and two of its impurities which were then used for calibration and calculation of the actual concentration. See figure 1 for an example chromatogram. The method was simple, accurate, reproducible, and selective.

In the paper DeAngelis describes a quantitative thin-layer chromatography (TLC) procedure for the analysis of the anticonvulsant cinromide (I, 3-bromo-N-ethylcinnamamide) [58473-74-8] and its 2 major metabolites, 3-bromocinnamamide [71539-43-0] and 3-bromocinnamic acid [32862-97-8], in plasma of the dog. These compounds were recovered from acidified plasma by extraction into benzene, with a recovery of 95%. All 3 compounds were quantitated directly on a TLC plate by UV absorbance densitometry at 270 nm. The linear range for the quantification of the compounds on a TLC plate was 10-1000 ng. The complete procedure is useful in the range 50-100 g/mL plasma, with a relative standard deviation of about 10%. The specificity of the method for the parent drug and each of its metabolites was confirmed by high-performance liquid chromatography. The method was used to determine the pharmacokinetics of cinromide and its 2 major plasma metabolites in dogs following a single oral dose of the drug. Pages 354-356 teach the preparation of standards of each of the compounds and the spotting of these standards and samples on to the TLC plates for quantification and verification of the samples.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the planar and liquid chromatography methods of Dreassi to determine stability/impurities in the tablet or other formulations of lamotrigine as taught by Floyd using standards of lamotrigine and its known impurities as taught by Floyd because as taught by

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Quaglia or DeAngelis standard compositions of the expected or known components in the composition assist in verifying and quantifying the components of pharmaceutical formulations.

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-2 and 11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,333,198. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims have a scope that completely encompasses the patented claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose telephone number is (703) 308-3989. The examiner's schedule is variable between the hours of about 5:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

For communication by fax to the organization where this application or proceeding is assigned, (703) 305-7719 may be used for official, unofficial or draft papers. When using this number a call to alert the examiner would be appreciated. Numbers for faxing official papers are 703-872-9310 (before finals), 703-872-9311 (after-final), 703-305-7718, 703-305-5408 and 703-305-5433. The above fax numbers will generally allow the papers to be forwarded to the examiner in a timely manner.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.



June 27, 2003

ARLEN SODERQUIST
PRIMARY EXAMINER